

CLAIMS

WHAT IS CLAIMED IS:

- 5 1. A polypeptide analog of a cationic polypeptide wherein the analog has an amino acid sequence that differs from the native sequence of the original polypeptide by one or more amino acid residues, or by chemical modification of one or more
10 amino acid residues in the native sequence, such that the isoelectric point is lower and the *in vivo* circulating life and/or absorption is increased for the analog relative to those same properties in the unmodified cationic polypeptide.
- 15 2. A polypeptide according to claim 1, which is also characterized by a lower charge under physiological conditions compared to the unmodified cationic polypeptide.
- 20 3. A polypeptide according to claim 1, which is an analog of a cationic protein selected from the group consisting of neurotrophic factor-3 (NT-3), brain derived neurotrophic factor (BDNF), macrophage growth
25 and differentiation factor (MGDF) and keratinocyte growth factor (KGF).
4. A polypeptide according to claim 3, which is an analog of NT-3.
- 30 5. A polypeptide according to claim 4, having the amino acid sequence of SEQ ID NO: 3.
6. A polypeptide according to claim 4, having
35 the amino acid sequence of SEQ ID NO: 5.

7. A polypeptide according to claim 4, having the amino acid sequence of SEQ ID NO: 6.
8. A polypeptide according to claim 4, having the amino acid sequence of SEQ ID NO: 7.
9. A DNA molecule encoding a polypeptide analog of a cationic polypeptide wherein the analog has an amino acid sequence that differs from the native sequence of the original polypeptide by one or more amino acid residues, or by chemical modification of one or more amino acid residues in the native sequence, such that the isoelectric point is lower and the *in vivo* circulating life and/or absorption is increased for the analog relative to those same properties in the unmodified cationic polypeptide.
10. A DNA molecule according to claim 9 which encodes an analog of a cationic protein selected from the group consisting of NT-3, BDNF, MGDF and KGF.
11. A DNA molecule according to claim 10 which encodes a polypeptide analog of NT-3.
12. A DNA molecule according to claim 11 which encodes the polypeptide of SEQ ID NO: 3.
13. A DNA molecule according to claim 11 which encodes the polypeptide of SEQ ID NO: 5.
14. A DNA molecule according to claim 11 which has the nucleic acid sequence of SEQ ID NO: 2.
15. A DNA molecule according to claim 11 which has the nucleic acid sequence of SEQ ID NO: 4.

16. A biologically functional expression vector which includes a DNA molecule according to claim 9 operatively linked to expression regulatory sequences.

5 17. A prokaryotic or eukaryotic host cell transformed or transfected with an expression vector according to claim 16 in a manner allowing the host cell to express the polypeptide encoded by the DNA molecule.

10

18. A transformed or transfected bacterial host cell according to claim 17.

15 19. A transformed or transfected *E. coli* host cell according to claim 18.

20 20. A transformed or transfected mammalian host cell according to claim 17.

21. A transformed or transfected CHO cell according to claim 20.

22. A transformed or transfected COS cell according to claim 20.

25

23. A process for the production of a polypeptide analog of a cationic polypeptide, wherein the analog has an amino acid sequence that differs from the native sequence of the original polypeptide by one or more amino acid residues, such that the isoelectric point is lower and the *in vivo* circulating life and/or absorption is increased for the analog relative to those same properties in the unmodified cationic polypeptide, said process comprising culturing under suitable nutrient conditions a prokaryotic or eukaryotic host cell transformed or transfected with an

30

35

expression vector comprising a DNA molecule encoding said polypeptide in a manner allowing the host cell to express the polypeptide, and optionally isolating the polypeptide product of the expression.

5

24. A process according to claim 23, in which the polypeptide is an analog of NT-3.

25. A process according to claim 23 in which the DNA molecule has been prepared by site directed mutagenesis.

10

15

26. A process according to claim 23, in which the analog has the amino acid sequence of SEQ ID NO: 3.

27. A process according to claim 23, in which the analog has the amino acid sequence of SEQ ID NO: 5.

28. A process according to claim 23, in which the analog has the amino acid sequence of SEQ ID NO: 6.

20

29. A process according to claim 23, in which the analog has the amino acid sequence of SEQ ID NO: 7.

30. A process according to claim 23, in which the host cell is bacterial.

25

31. A process according to claim 30, in which the bacterial host cell is *E. coli*.

30

32. A polypeptide product of expression in a eukaryotic or prokaryotic host cell of a DNA molecule according to claim 9.

33. An antibody against a polypeptide according to claim 1.

35

34. An antibody according to claim 33 which is polyclonal.

5 35. An antibody according to claim 34 which is monoclonal.

36. A pegylated derivative of a polypeptide according to claim 1.
10

37. A pharmaceutical composition comprising a therapeutically effective amount of a polypeptide according to claim 1 and a pharmaceutically acceptable carrier or diluent.
15

38. A method for the treatment of peripheral neuropathies, comprising administering to a patient having the disorder a therapeutically effective amount of a polypeptide according to claim 4.
20